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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,527	12/27/2001	Raymond L. Houghton	210121.513C1	7914

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/033,527	HOUGHTON ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,40,41 and 44-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37,41 and 44-46* is/are rejected.

7)☒ Claim(s) *40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed August 6, 2007 is acknowledged and has been entered. Claims 1-36, 38-39, 42 and 43 have been canceled. Claims 37, 41, 45 and 46 have been canceled. All of the arguments have been thoroughly reviewed and considered, but are deemed moot in view of the new grounds of rejections necessitated by Applicant's amendment of the claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections and Objections

3. The prior art rejections under 35 USC 102(e) are withdrawn in view of Applicant's amendment of the claims. The objection to the claims 44 is withdrawn in view of the new grounds of rejections.

New Ground(s) of rejection

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 37 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frudakis et al (reference made of record in prior Office action) in view of Weaver et al (citation made of record in the prior art). Regarding claims 37 and 41, Frudakis et al teach a composition for detecting a breast cancer cell in a biological sample of a patient, said composition comprising (a) a first oligonucleotide, (b) a second oligonucleotide, wherein said first oligonucleotide and said second oligonucleotide hybridize to a first polynucleotide, or the complement thereof and to a second polynucleotide or the complement thereof, respectively, wherein said first polynucleotide and said second polynucleotide comprise a sequence depicted in SEQ ID NO: 7 (see SEQ ID NO: 303, col. 9, lines 26-29; col. 14, 18-24 and 40-62; and col. 21, lines 27-50). Frudakis et al teach wherein the composition may have more than one oligonucleotide pair (col. 14).

Frudakis et al does not teach wherein the composition comprises an oligonucleotide or oligonucleotide pair that hybridizes to the sequence of SEQ ID NO: 75 or the complement thereof.

Weaver teaches a composition for detecting breast cancer cells in a biological sample, said composition comprising (a) a first oligonucleotide (b) a second oligonucleotide; wherein said first and second oligonucleotide hybridize to a first polynucleotide, or the complement thereof, and to a second polynucleotide or the complement thereof respectively, wherein said first and second polynucleotide comprise a sequence depicted in SEQ ID NO: 75 (See SEQ ID NO: 1034, paragraphs 0053, 0073, 0081, 0082, and 0090). Weaver et al teaches wherein the sequence recited therein are genes that are up-regulated in cancer cells relative to normal cells. Weaver et al teach that the gene pattern resulting from these genes, such as those encompassing the sequence depicted in SEQ ID NO: 75 (SEQ ID NO: 1034) are indicative of a cancerous state and thus have potential for development of antitumor agents (see 0081 and 0082).

In view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have provided a composition comprising oligonucleotides which hybridizes to a sequence comprising the sequence of SEQ ID NO: 7 and 75 for the benefit of providing gene patterns indicative of a cancerous state in biological sample and for the benefit of developing potential antitumor agents as suggested by Weaver et al.

6. Claims 44 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frudakis et al in view of Weaver et al and in view of Shimkets et al (WO 01/47944 A2, July 2001) and further in view of Buck et al (Biotechniques, Vol. 57, pages 528-536,

September 1999). Regarding claims 44 and 46, Frudakis et al in view of Weaver et al teach the composition of claim 41 as previously discussed above.

They do not teach wherein the oligonucleotides are selected from the group consisting of oligonucleotides as depicted in SEQ ID NOS: 53-57.

Shimkets et al teach a primer sequence that is 80% identical to the sequence of SEQ ID NO: 53 (see SEQ ID NO: 51, see alignment below). Shimkets et al teach the use of the sequence as oligonucleotides useful in hybridization reactions (page 5).

1 CAATTTTGGTGGAGAA 16 (SEQ ID NO: 53 of the instant invention).
8 CAATTTTGGTGGAGAA 23 (SEQ ID NO: 51 of Shimkets).

The primer of the instant invention only differs from the primer of Shimkets of et al by addition of a few bases at the 5' end and/or 3' end.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers and probes simply represent structural homologs of the oligonucleotides taught by Shimket et al, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the

claimed oligonucleotide is *prima facie* obvious over the cited references in the absence of secondary considerations.

With regard to the issue of equivalence of the primers, MPEP 2144.06 notes "Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982)."

With regard to the issue of reasonable expectation of success in using such equivalents, Buck et al expressly provides a general teaching of evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18-mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the

primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region.

This clearly shows that every primer would have a reasonable expectation of success.

7. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer et al (6489146, effective filing date in view of Buck et al as previously cited above. Regarding claims 45 and 46, Stemmer et al teach a composition (see col. 1, "technical field) comprising a sequence wherein said sequence comprises 12 consecutive nucleotides that are identical to the oligonucleotide of SEQ ID NO: 57 (see oligonucleotide recited in SEQ ID NO: 36; see alignment below).

5 GACTTGCTGTTTTTGCTC 22 instant invention
7 GCCTTCCTGTTTTTGCTC 24 SEQ ID NO: 36

The primer of the instant invention only differs from the primer of Stemmer et al by addition of a few bases at the 5' end and/or 3' end.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers and probes simply represent structural homologs of the oligonucleotides taught by Stemmer et al, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed oligonucleotide is *prima facie* obvious over the cited references in the absence of secondary considerations.

With regard to the issue of equivalence of the primers, MPEP 2144.06 notes "Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982)."

With regard to the issue of reasonable expectation of success in using such equivalents, Buck et al expressly provides a general teaching of evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3); with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the

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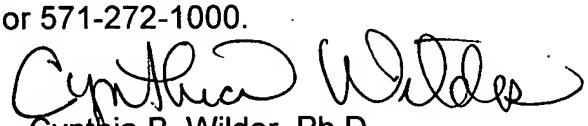
This clearly shows that every primer would have a reasonable expectation of success.

Conclusion

8. Claims 37, 41, 44-46 are rejected. Claim 40 is objected because it depends from a rejected claim. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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Patent Examiner
Art Unit 1637

10/2/2007